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# CATECHOLAMINE EXCRETION IN HEAT-ACCLIMATIZED MEN

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## **FOREWORD**

**This report was prepared by the following personnel in the Physiology Branch:**

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## ABSTRACT

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Sympathoadrenal activity was appraised in 10 healthy men over a 10-week period, beginning in summer and ending in autumn. Two overnight urine samples per subject per week were analyzed for norepinephrine, epinephrine, creatinine, and urea. Evidence of high sympathoadrenal activity was obtained in summer, with reversal in autumn. The different catecholamines were shown to relate either to weekly mean maximum temperature, to weekly mean solar radiation, or to both climatic factors. Catecholamine excretion also tended to vary inversely with urea excretion, which may be interpreted as indicating interaction between catecholamines and thyroid hormone, the latter possibly modifying metabolic actions of the former. The results also may be interpreted as indicating that catecholamines contribute to the regulation of blood distribution, a function of major importance in heat acclimatization.

This technical documentary report has been reviewed and is approved.

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## CATECHOLAMINE EXCRETION IN HEAT-ACCLIMATIZED MEN

### 1. INTRODUCTION

In Aerospace Medicine there is a continuing interest in the physiology of heat stress and heat acclimatization, since there are situations in which flying or ground personnel cannot avoid heat exposure. The gains in heat tolerance that result from repeated or long-term exposure to hot environments have been shown to relate to cardiovascular adaptations (1); these, in turn, depend upon adjustments in regulatory mechanisms, both neural and hormonal (2). The catecholamines, epinephrine and norepinephrine, have been shown to contribute to heat tolerance; the evidence for this comes from acute experiments on small mammals (3-6). In the present investigation, the effect of chronic exposure to heat on the sympathoadrenal system was studied in human subjects by means of urinary catecholamine determinations.

### 2. METHODS

Ten healthy men were studied. All were members of the laboratory staff and, therefore, had the same daily work schedule and were subject to the same environmental conditions during work periods. All were accustomed to outdoor exercise. The study began in late summer, when daily maximum temperatures were still as high as 95° F. (35° C.); it ended 10 weeks later, when temperature maximums no longer exceeded comfort levels.

Timed, overnight urine samples collected each Wednesday and Thursday were analyzed for norepinephrine, epinephrine, and creatinine. The urine was acidified immediately upon collection by adding 12 normal HCl (2 ml./250 ml.

urine) and then stored in the frozen state. The catecholamines were determined by a modification of the trihydroxyindole method (7), and creatinine determinations were made with the AutoAnalyzer.

The average of the two values obtained each week for each urinary constituent for each subject was taken as his weekly value, and statistical appraisal was performed using the weekly values. Covariance analysis was performed, with maximum outdoor temperature and solar radiation as covariates. The weekly mean maximum temperature and weekly mean solar radiation (Langley) values were obtained from the U.S. Weather Bureau. In analyzing the data, the catecholamines were expressed both as hourly excretion rates and as ratios with creatinine.

### 3. RESULTS

The climatic and physiologic data have been presented in the form of time-course curves in figure 1. Temperature maximums for the 30 days preceding the period of study had averaged 95° F., with relative humidity averaging 35% at the time the temperature was maximal. Temperature tended to be relatively high during the first 4 weeks of the study period; it fell progressively during the final 6 weeks. Of importance is the dissimilarity in the patterns of change for maximum temperature and solar radiation.

Through covariance analysis, epinephrine (expressed either as hourly excretion rate or as the ratio with creatinine) was shown to relate to maximum temperature. Norepinephrine (when expressed as excretion rate) also related to temperature; when expressed as the ratio with creatinine, it related to solar radiation.

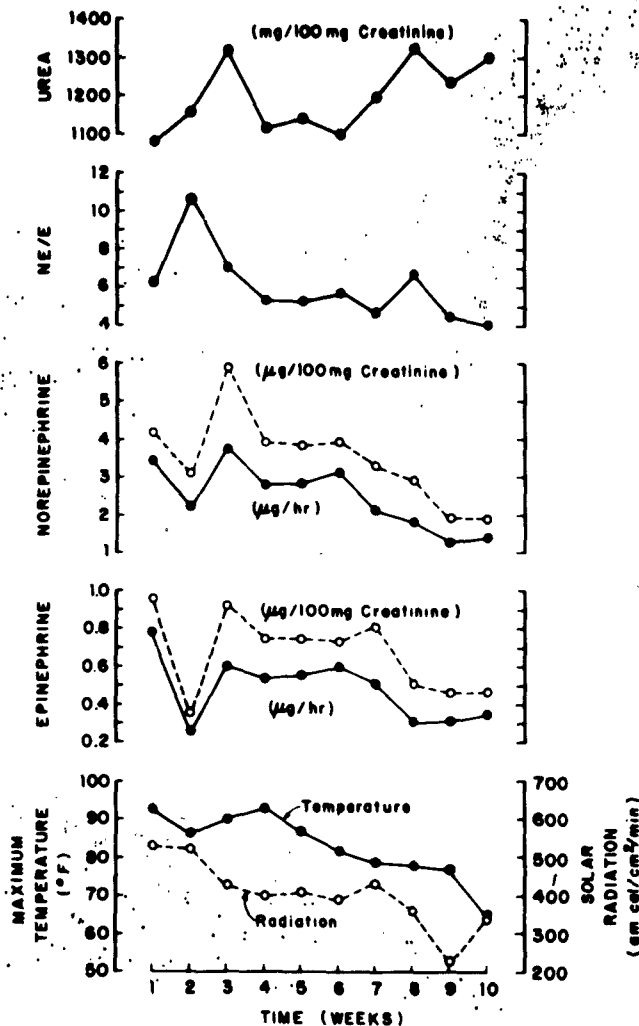


FIGURE 1

*Time-course curves.*

The NE/E ratio also related to solar radiation. There was, however, significant time variability for each of these variables that was not accounted for by changes in temperature or radiation. Table I presents significance levels for the reduction in variability due to the covariate (regression) and the significance levels for the unaccounted variability (deviation from regression).

Since deacclimatization changes could be expected during the period of temperature decline, a special analysis was performed on the

data obtained in weeks 4 to 10. During this particular period, epinephrine (either as rate or as ratio) related to solar radiation, and there was no unaccounted variability. Both temperature and solar radiation were required to explain the variability for norepinephrine. Temperature alone was as good as both covariates for the NE/E ratio, but there was significant unaccounted-for variability.

The time trends brought out by plotting the mean values for the 10 subjects (fig. 1) are

TABLE I  
Statistical data—significance levels

Urinary determination	Regression	Deviation from regression	Covariate
Epinephrine (as rate)	.005	.01	Temperature
Epinephrine (as ratio)	.05	.05	Temperature
Norepinephrine (as rate)	.001	.005	Temperature
Norepinephrine (as ratio)	.005	.01	Radiation
Norepinephrine/epinephrine	.001	.01	Radiation

of interest, because they show that the patterns of change were essentially the same when the catecholamines were expressed as ratios with creatinine or as hourly excretion rates. It can also be seen that the catecholamines, when expressed as ratios, consistently run higher than when expressed as rates.

In addition, epinephrine and norepinephrine showed high positive correlation. The between-subject correlation was .98, which differed significantly from zero ( $P < .001$ ); the within-subject correlation coefficient was .83 with  $P < .001$ . It may, therefore, be concluded that different parts of the sympathoadrenal system were influenced proportionately by climatic factors.

#### 4. DISCUSSION

With the exception of the values obtained in the second week, these data provide evidence of relatively high sympathoadrenal activity in late summer and a decrease in autumn. The aberrancy in the second week cannot be ignored, but it is not destructive to the general conclusion offered. The change in the second week appears to be a response to temperature reduction, since this was the first week in 3 months that daily temperatures had not exceeded 90° F.

The finding that the progressive declines in epinephrine and norepinephrine excretion started later than the progressive temperature decline provides evidence of acclimatization. The lag period for norepinephrine was 2 weeks, and that for epinephrine was 3 weeks. There

is, therefore, agreement between these results and those of Bean and Eichna (8), who found, by other means, that deacclimatization changes begin about 2 weeks after heat exposure is discontinued.

Of importance is the finding that catecholamine excretion tended to level off when maximum temperatures no longer exceeded 80° F. It seems, therefore, that a new steady state was developing, which was manifested earlier in epinephrine than in norepinephrine. The final values were compared with ones reported by other investigators (9, 10), who also analyzed overnight urine and expressed catecholamines as ratios with creatinine. The final norepinephrine value in the present study was 1.94  $\mu\text{g./100 mg. creatinine}$ ; these other investigators reported 1.68 and 1.25. The corresponding epinephrine values were 0.47, 0.06, and 0.19  $\mu\text{g./100 mg. creatinine}$ . The second value in each series represents subjects studied in winter, and the third value in each series represents subjects not receiving fruit and caffeine-containing and vanilla-containing food (season was not indicated). It, therefore, seems that the late autumn values in the present study are near-basal values. An additional study is now in progress to determine basal values in this climate; in the variation in catecholamine excretion over four seasons is being determined.

Additional information is available for these 10 subjects. The urine samples collected over the 10-week test period were also analyzed for sodium, potassium, phosphate, urea, uric acid, and 17-hydroxycorticosteroids (17-OHCS). These results have been reported separately (11). No significant seasonal variation was

found for sodium or uric acid, but potassium, phosphate, and urea (when expressed as ratios with creatinine) showed significant upward shifting, and the 17-OHCS/creatinine ratio showed significant downward shifting during the period of temperature decline. These trends were established using data for 21 subjects, not just the 10 considered in the present effort. The 10 in the present study represent only those of the original group whose exercise habits did not vary over the 10-week experimental period.

The urea/creatinine curve for these 10 subjects has been presented in figure 1. Except for one aberrant value, which appeared in the third week, these results indicate relative metabolic depression up to and including the sixth week, with an upward shift finally. This same summer-autumn variation in the urea creatinine ratio was found in an earlier study (12), in which daytime urine, rather than nighttime urine, was analyzed. One interpretation is that thyroid activity was relatively low in summer. The literature on the depressant effect of chronic heat on the thyroid was reviewed previously (11).

The finding of an inverse relationship between urea and catecholamine excretion is interesting, since Soffer et al. (13) found evidence of thyroid depression (decreased uptake of  $I^{131}$ ) in rats treated with epinephrine. In addition, they showed that adrenocorticosteroids contributed to this response. Judging by urea excretion, gluconeogenesis was lower in the present subjects in summer than in autumn, although catecholamines were higher in summer than in autumn. Apparently, high sympathoadrenal activity in summer did not unduly affect carbohydrate metabolism. Knowing that heat-acclimatized persons have normal body temperatures, it seems unlikely that the catecholamines had their usual calorogenic action. Gellhorn and Feldman (4) noted, in acutely heat-stressed rats, that adreno-demodulation led to hypoglycemia, but this could be prevented by vagotomy, and vagotomy alone led to hyperglycemia in heat-stressed rats. Kubicek et al. (6) found that sympathecto-

mized dogs experienced more marked hypoglycemia during hyperthermia than did intact dogs, and circulatory collapse occurred more frequently after sympathectomy. This latter observation is of interest, since circulatory collapse occurs frequently when persons who are not acclimatized to heat attempt vigorous activity in hot environments.

The level of circulating thyroid hormone is considered a major factor determining responsiveness to administered epinephrine (14). The present results suggest that chronic exposure to heat induces high secretion of catecholamines, but through a counterbalancing mechanism involving the thyroid, metabolic sensitivity to catecholamines may become reduced.

Others have studied the effects of acute heat exposure on the human. Berman et al. (15) found no evidence of high catecholamine release in human subjects exposed to 130° F. (54° C.) air temperature. Hasselman et al. (16) reported that high ambient temperature (37° to 40° C.) per se did not increase the urinary excretion of epinephrine or norepinephrine in human subjects. Ambient temperature had an effect on excretion of catecholamines only when in combination with sleep deprivation; the increase associated with sleep deprivation was less marked at high temperatures than at low temperatures; and excretion levels during sleep were lower after work at high temperatures than after work at low temperatures.

Much work has been done on circulatory adjustments to heat. In a recent study (17), reactions in peripheral tissues were examined in nonacclimatized human subjects who were working in heat. Excess lactate appeared at work loads which did not produce excess lactate in the absence of heat. This was interpreted as indicating that a greater fraction of the cardiac output was shunted away from muscle to skin during work in heat. In persons who are acclimatized to heat (and by definition this means that they have high work capacity in heat), blood flow to skin and to muscles must be highly regulated, since heat dissipation is

efficient and work capacity is high. It has long been known that catecholamines can cause vasodilatation in skeletal muscle and vasoconstriction in skin. The finding of relatively high catecholamine excretion in heat-acclimatized men lends support to the long-standing hypothesis that catecholamines contribute to

the regulation of blood distribution. Although the evidence is indirect, it appears that possible adverse metabolic effects of such high catecholamine secretion are offset by changes in other endocrine glands, particularly the thyroid.

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<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-63-20. CATECHOLAMINE EXCRETION IN HEAT-ACCLIMATIZED MEN. Mar. 63, 5 pp. incl. illus., table, 17 refs.</p> <p>Sympathoadrenal activity was appraised in 10 healthy men over a 10-week period, beginning in summer and ending in autumn. Two overnight urine samples per subject per week were analyzed for norepinephrine, epinephrine, creatinine, and urea. Evidence of high sympathoadrenal activity was obtained in summer, with reversal in autumn. The different catecholamines were shown to relate either to weekly mean maximum temperature, to weekly</p>	<p>1. Catecholamine excretion 2. Heat acclimatization</p> <p>I. AFSC Task 775801 II. H. B. Hale, E. W. Williams, J. P. Ellis, Jr. III. In ASTIA collection</p>	<p>USAF School of Aerospace Medicine, Brooks AF Base, Tex.</p> <p>SAM-TDR-63-20. CATECHOLAMINE EXCRETION IN HEAT-ACCLIMATIZED MEN. Mar. 63, 5 pp. incl. illus., table, 17 refs.</p> <p>Sympathoadrenal activity was appraised in 10 healthy men over a 10-week period, beginning in summer and ending in autumn. Two overnight urine samples per subject per week were analyzed for norepinephrine, epinephrine, creatinine, and urea. Evidence of high sympathoadrenal activity was obtained in summer, with reversal in autumn. The different catecholamines were shown to relate either to weekly mean maximum temperature, to weekly</p>	<p>1. Catecholamine excretion 2. Heat acclimatization</p> <p>I. AFSC Task 775801 II. H. B. Hale, E. W. Williams, J. P. Ellis, Jr. III. In ASTIA collection</p>
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